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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/718,403	11/20/2003	Steffen Breitfelder	1/1423	9746

28501 7590 06/30/2004

BOEHRINGER INGELHEIM CORPORATION
900 RIDGEBURY ROAD
P. O. BOX 368
RIDGEFIELD, CT 06877

EXAMINER	
HUANG, EVELYN MEI	

ART UNIT	PAPER NUMBER
1625	

DATE MAILED: 06/30/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/718,403	BREITFELDER ET AL.	
	Examiner	Art Unit	
	Evelyn Huang	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-29 is/are pending in the application.

4a) Of the above claim(s) 22-24 is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-6,8-10,12-14,16-21 and 25-27 is/are rejected.

7)☒ Claim(s) 7,11,15,28 and 29 is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-21, 25-29, drawn to a compound of formula 1, classified in class 546, subclass various dependent on the species elected, and the composition thereof.

II. Claim 22, drawn to a composition comprising multiple active ingredients, classified in class 514, subclass various dependent on the species elected

III. Claims 23-24, drawn to multiple method of use, classified in class 514, subclass various dependent on the species elected.

The inventions are distinct, each from the other because of the following reasons:

Inventions I and III are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case, the product as claimed can be used in a materially different processes, such as in the treatment of asthma, heart rhythm disorders, spasms in the gastrointestinal tract etc.

The patentability of Group II invention depends on the type and amount of the multiple active ingredients, their interaction, co-action, e.g. synergism etc., which is patentably distinct from the Group I composition containing only a single active ingredient.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art because of their recognized divergent subject matter, the search required for one group of invention is not required for the other groups, restriction for examination purposes as indicated is proper.

2. During a telephone conversation with Mr. Witkowski on 6-22-2004 a provisional election was made with traverse to prosecute the invention of Group I, claims 1-21, 25-29. Affirmation of this election must be made by applicant in replying to this Office action. Claims of Group II and III inventions are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

3. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to

retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.**

Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-21, 25-29 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. It is unclear whether the claims are directed to a compound or to a mixture of the compound and the pharmaceutically acceptable salts thereof. Amending the claims to singular/alternative format is recommended, i.e. A compound.....or the pharmaceutically acceptable salt thereof'.

b. Claims 16-19, the term 'benzhydryl' has no antecedent basis in their respective base claims, wherein only 'benzyl' is described.

The rejection is applicable to claims dependent on the above claims.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 1-4, 8, 12, 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over King (4797387)

King generically discloses an azabicyclic compound with 5-HT antagonist activity, and the pharmaceutical composition thereof (columns 1-2, formula I). A specific compound is described (column 2, Example 4, compound E4).

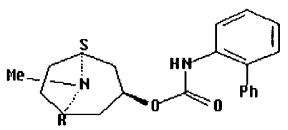
King's E4 compound is the non-quaternized form of the instant compound.

King, however, teaches that the E4 compound may be in the quaternized salt form, which is an example of the pharmaceutically acceptable salts (column 3, lines 5-14).

At the time of the invention, one of ordinary skill in the art would be motivated to prepare the quaternized salt form of King's E4 compound to arrive at the instant invention since King had expressly taught that the compound or its pharmaceutically acceptable salt, such as the quaternized salt, would be useful as a 5-HT antagonist for treatment of migraine or emesis.

7. Claims 1-4, 8, 12, 16, 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Takeuchi (EP 747 355)

Takeuchi generically discloses an azabicyclic carbamate compound with M3 antagonist activity, and the pharmaceutical composition thereof (pages 4-5, formula I). A specific compound is described (page 50, Example 58).



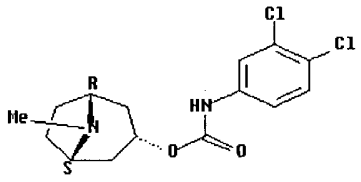
Takeuchi's compound is the non-quaternized form of the instant compound.

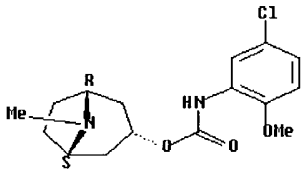
Takeuchi, however, specifically teaches that the inventive compound may be in the quaternized salt form (page 5, lines 15-34, definition of Z). Examples are shown on page 52 for compounds 2, 4.

At the time of the invention, one of ordinary skill in the art would be motivated to prepare the quaternized salt form of Takeuchi's compound to arrive at the instant invention since Takeuchi had expressly taught that the inventive compound or its quaternized salt, would be useful as a M3 antagonist useful in the treatment of gastrointestinal, respiratory or urinary diseases.

8. Claims 25-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mach (6113877)

Mach generically discloses an azabicyclic compound as a sigma 2 specific ligand (columns 1-2, formula I). Specific compounds are described (column 6, Examples 2-3) with the following structures.





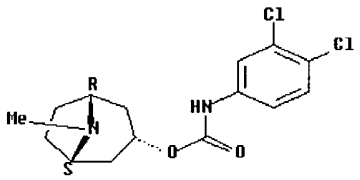
The instant compound has a -CH=CH- or -$(CH_2)_3$ – as A where as Mach's Examples 2-3 have -$(CH_2)_2$ – as X (corresponding to the instant A).

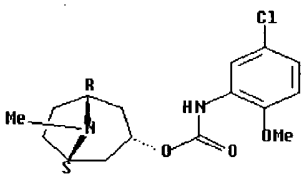
Mach, however, teaches that -CH=CH- or -$(CH_2)_3$ – , -$(CH_2)_2$ – are optional choices (column 1, line 54, definition of X).

At the time of the invention, one of ordinary skill in the art would be motivated to replace the -$(CH_2)_2$ – with the alternative -CH=CH- or -$(CH_2)_3$ – to arrive at the instant invention, with the reasonable expectation of obtaining an additional sigma 2-specific ligand for assaying the presence of sigma 2 receptors.

9. Claims 1-6, 8-10, 12-14, 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mach (6113877) in view of King (4797387) and/or Takeuchi (EP 747 355) and/or Banholzer (5770738).

Mach generically discloses an azabicyclic compound as sigma 2 specific ligand (columns 1-2, formula I). Specific compounds are described (column 6, Examples 2-3) with the following structures.





Mach's Examples 2-3 are the Takeuchi's compound is the non-quaternized form of the instant compound.

However, Mach teaches that the inventive compound may be in the form of the pharmaceutically acceptable salt. The quaternized salts are art recognized pharmaceutically acceptable salts, as specifically taught by King (column 3, lines 5-14), and exemplified as optional choices for the azobicyclo [3.2.1]-octane compound (Takeuchi, page 5, lines 15-34 ; Banholzer, column 2, lines 35-48)

At the time of the invention, in view of the teachings of Mach, Takeuchi an d Banholzer, one of ordinary skill in the art would be motivated to prepare the quaternized salt form of Mach's compound to arrive at the instant invention, with the reasonable expectation of obtaining an additional sigma 2 specific compound for assaying the presence of sigma 2 receptors.

The compound of instant claims 5, 6, 9, 10, 13, 14 has a -CH=CH- or $-(CH_2)_3-$ as A where as Mach's Examples 2-3 have $-(CH_2)_2-$ as X (corresponding to the instant A).

Mach, however, teaches that -CH=CH- or $-(CH_2)_3-$, $-(CH_2)_2-$ are optional choices (column 1, line 54, definition of X).

At the time of the invention, one of ordinary skill in the art would be motivated to replace the $-(CH_2)_2-$ with the alternative -CH=CH- or $-(CH_2)_3-$ to arrive at the instant invention, with the reasonable expectation of obtaining an additional sigma 2 specific compound for assaying the presence of sigma 2 receptors.

Allowable Subject Matter

10. Claims 7, 11, 15, 28, 29 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. The subject matter of claims 17-19 (subjected to 112 (2) rejection) is also allowable.

The closest prior art is Mach (6113877). See paragraphs 8, 9 above. The recited substitutents on the phenyl of R4 in the instant compound (A is -CH=CH-, $-CH_2-O-CH_2-$ or $-(CH_2)_3-$) set a further demarcation from Mach's Examples 2-3. Motivation to modify Mach's example compounds via multiple changes to arrive at the instant is lacking.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Evelyn Huang whose telephone number is 571-272-0686. The examiner can normally be reached on Tuesday-Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph McKane can be reached on 571-272-0699. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Evelyn Huang
Primary Examiner
Art Unit 1625